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Comments on Published Studies

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Clinical assessment of the use of antiangiogenic eye drops

Avaliação clínica do uso de colírios de antiangiogênico

Evaluación clínica del uso de colirios de antiangiogénico

Shortened title: Antiangiogenic eye drops

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Pathological angiogenesis is the crux of the progression of wet age-related macular degeneration (AMD). To treat this choroidal neovascularization, vascular endothelial growth factor (VEGF) inhibitors (bevacizumab and ranibizumab)[1] and VEGF-trap (aflibercept) have been successfully used.[2] However, treatment with monthly injections is often required for better management of the pathology, which translates into high costs (financial, length of treatment, and mobilization of family members).[3] In this context, various drugs are being tested for AMD. In a previous phase II study with pazopanib eye drops at 5 mg/mL three times a day, an improvement in best-corrected visual acuity (BCVA) was observed in patients with exudative AMD.[4] The present multicenter, randomized, double-blinded study aimed to assess the efficacy of the use of pazopanib eye drops as an adjuvant therapy in the treatment of exudative AMD.

The authors hypothesized that the use of pazopanib (a tyrosine kinase inhibitor that inhibits VEGF receptors 1, 2, and 3 as well as the pro-angiogenic pathway of the platelet-derived growth factor) could be a noninvasive method to maintain or improve visual acuity and decrease the number of intravitreal injections. In this study, pazopanib eye drops were used in patients with exudative AMD. A total of 510 patients received baseline ranibizumab injections to avoid delaying treatment and to standardize them. Treatment regimens lasted for 52 weeks, and patients were divided into seven groups: pazopanib 5 mg/mL three times per day, pazopanib 5 mg/mL four times per day, pazopanib 10 mg/mL two times per day, pazopanib 10 mg/mL three times per day, pazopanib 10 mg/mL four times per day, placebo drops four times a day, and ranibizumab injection every 4 weeks. In the pazopanib and placebo groups, reinjections were administered on an as-needed basis. The objective was to evaluate the benefit of a noninvasive intervention with different dosages and application frequencies that was aimed at maintaining or even improving eyesight and decreasing the number of intravitreal injections. In addition, the plasma concentrations of pazopanib were measured and complement factor H genotypes were assessed to determine whether a better therapeutic response was obtained with pazopanib.

Palavras-chave:
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The primary efficacy endpoint of the study was alteration in BCVA over the 52-week treatment period. Secondary efficacy endpoints were the number of ranibizumab reinjections; moment of first reinjection; and presence of or alterations in fluids, cysts, or PED. [Remark 1] The minimum success criterion was noninferiority of the monthly ranibizumab injections [Remark 2] in BCVA (with a margin of five letters) with a decrease in 50% of ranibizumab injections on an as-needed basis.

As a result, pazopanib was well tolerated by the patients but had no therapeutic benefit compared with ranibizumab alone. In addition, at the end of 52 weeks, treatment with pazopanib and the placebo associated with ranibizumab injections on an as-needed basis was not worse than that with monthly ranibizumab injections alone. The minimum success criterion was not achieved because pazopanib therapy did not decrease the number of ranibizumab injections on an as-needed basis by more than 50%. Furthermore, complement factor H had no effect on pazopanib or ranibizumab response (BCVA, frequency of injections, or alterations on optical coherence tomography and angiography).

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